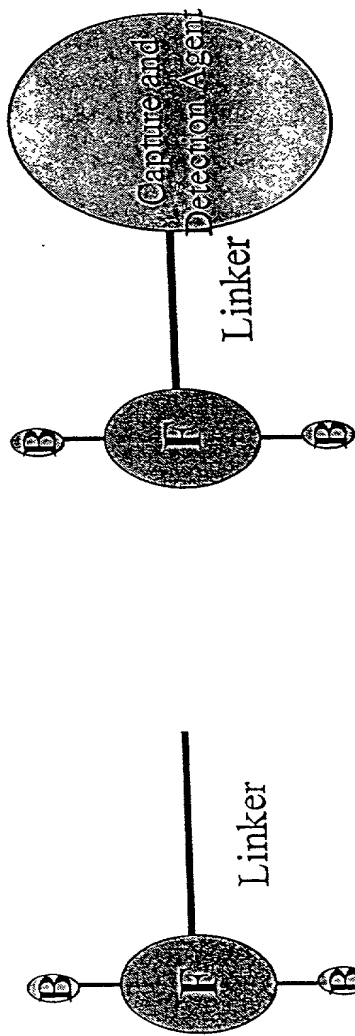
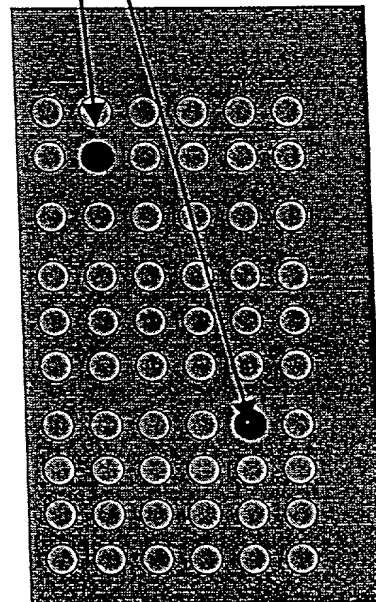


High-throughput Target ID



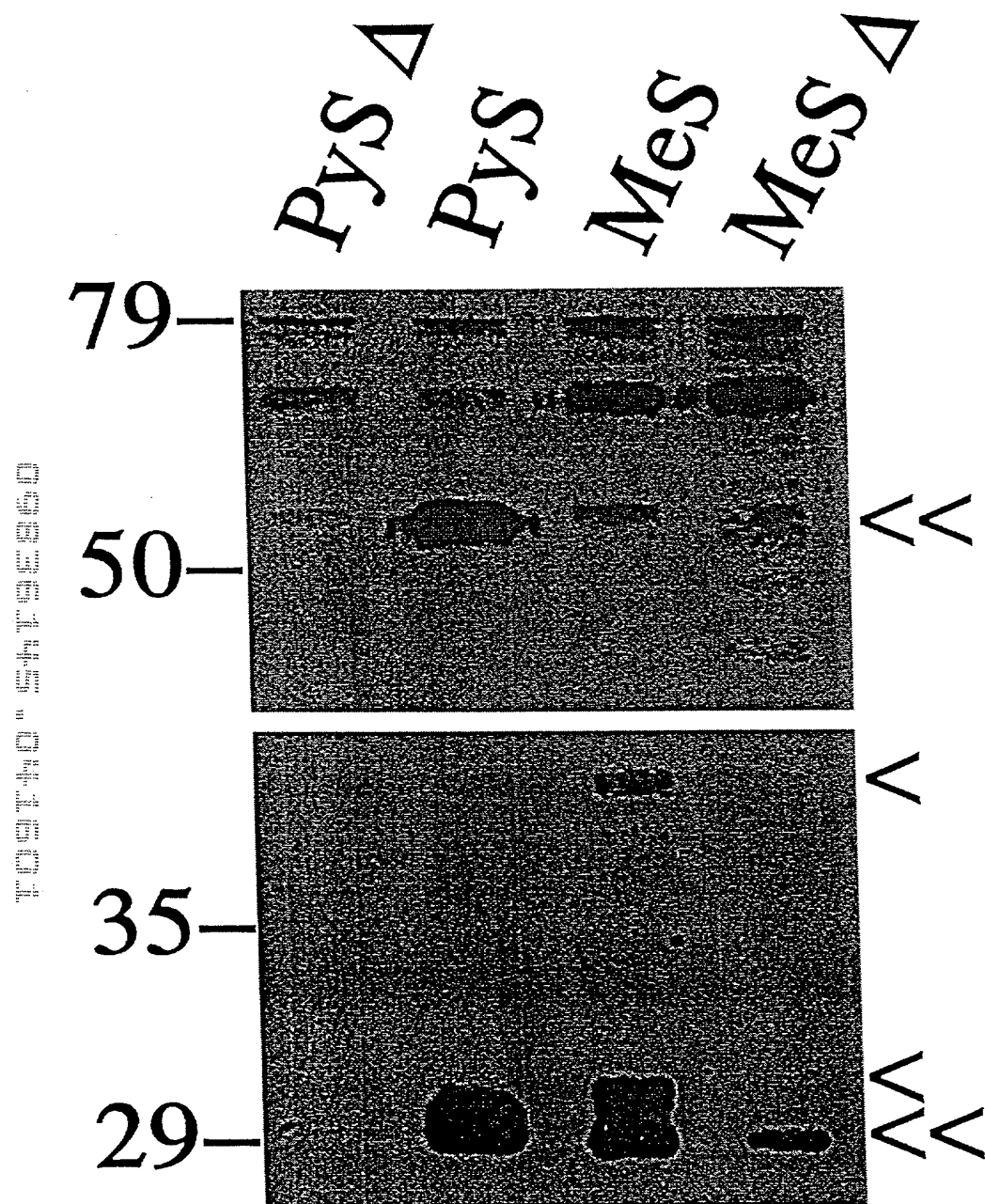
Library of Bioactive Compounds

Library of Target ID Compounds

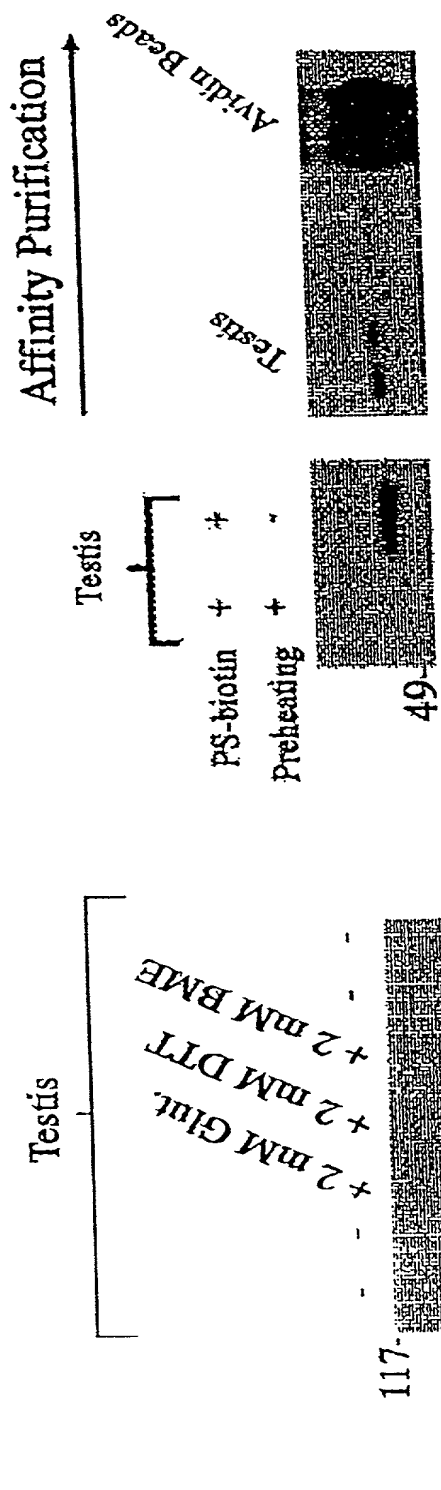


Use corresponding activity-based probe to identify the biological target

FIGURE 2



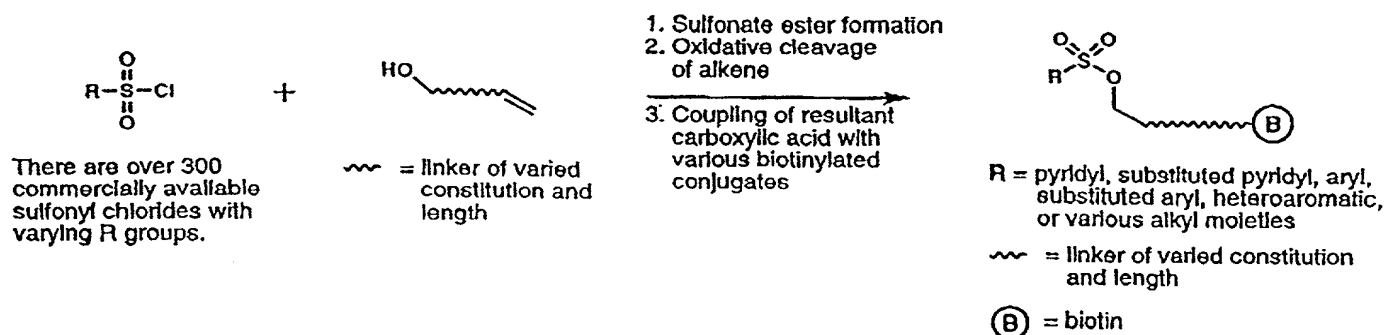
Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes



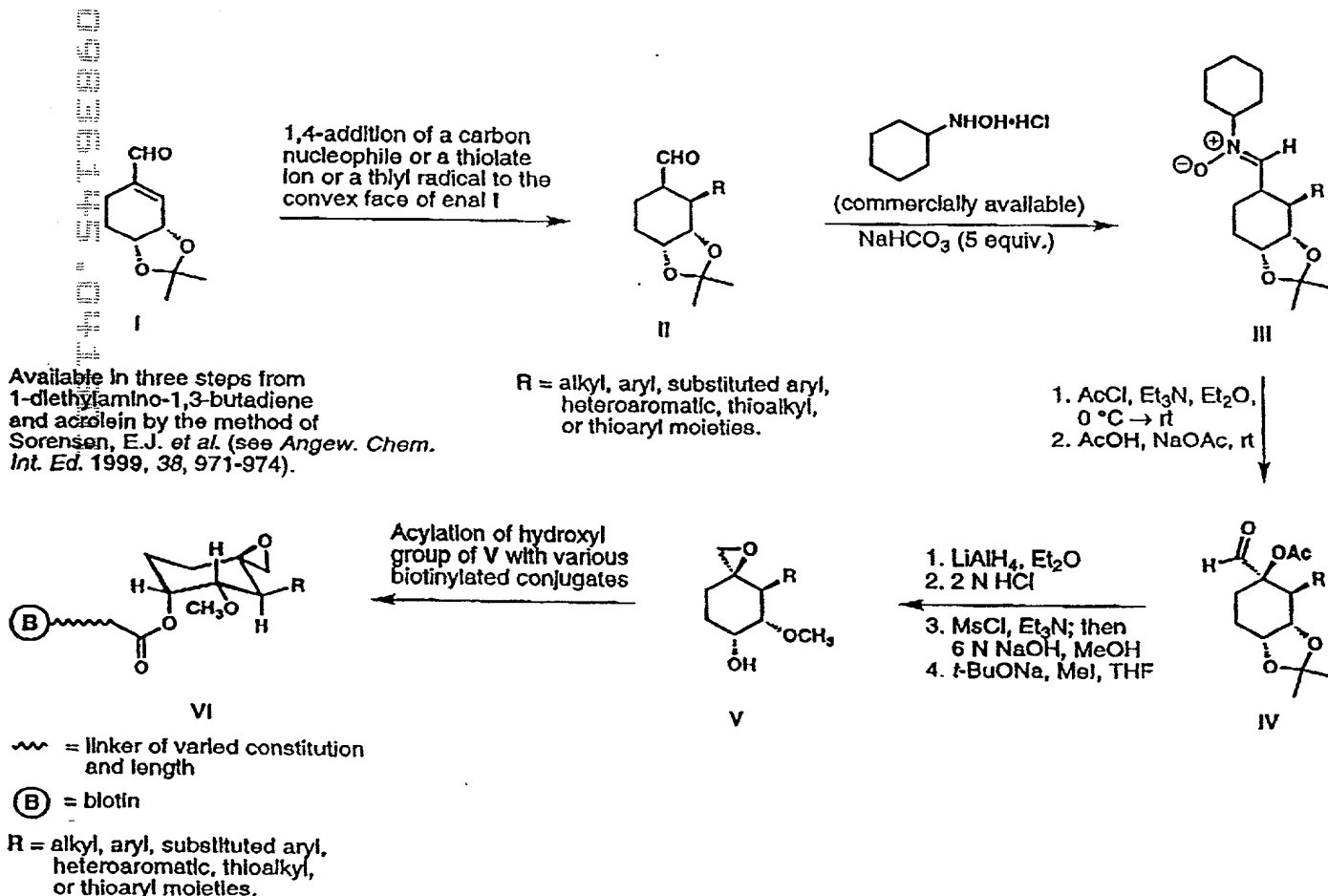
- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)
- 28 ADHs in fly genome
 - Involved in retinoic acid biosynthesis and catabolism of alcohol and chemotherapeutic agents

FIGURE 3

FIGURE 4



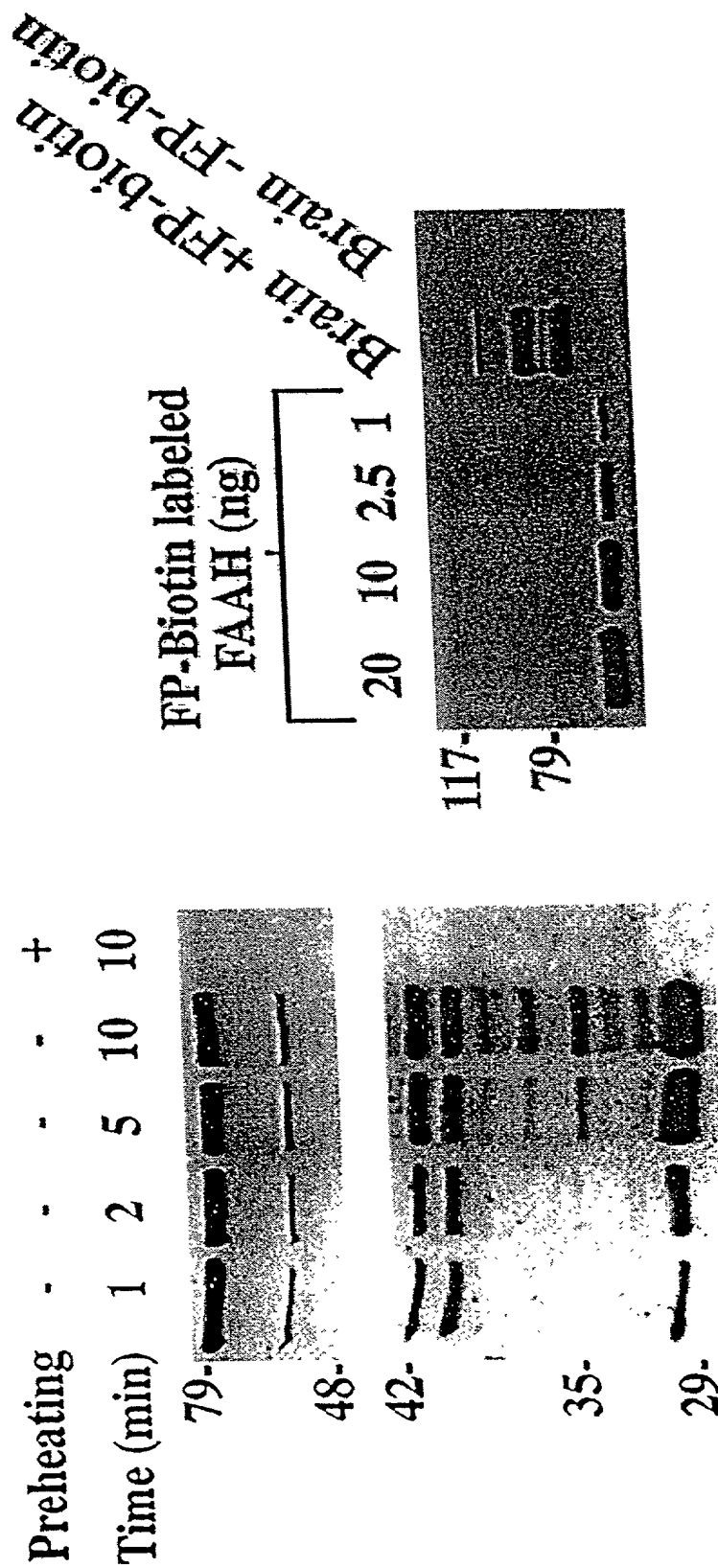
Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I → II → III → IV → V can be found in Sorensen, E.J. *et al. Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

FP-Biotin: a kinetic reporter of SH Activity

- The rates at which the majority of SHs react with FP-biotin can be experimentally followed
- FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes



Utility of Multiplexed probes in identifying Serine Hydrolases

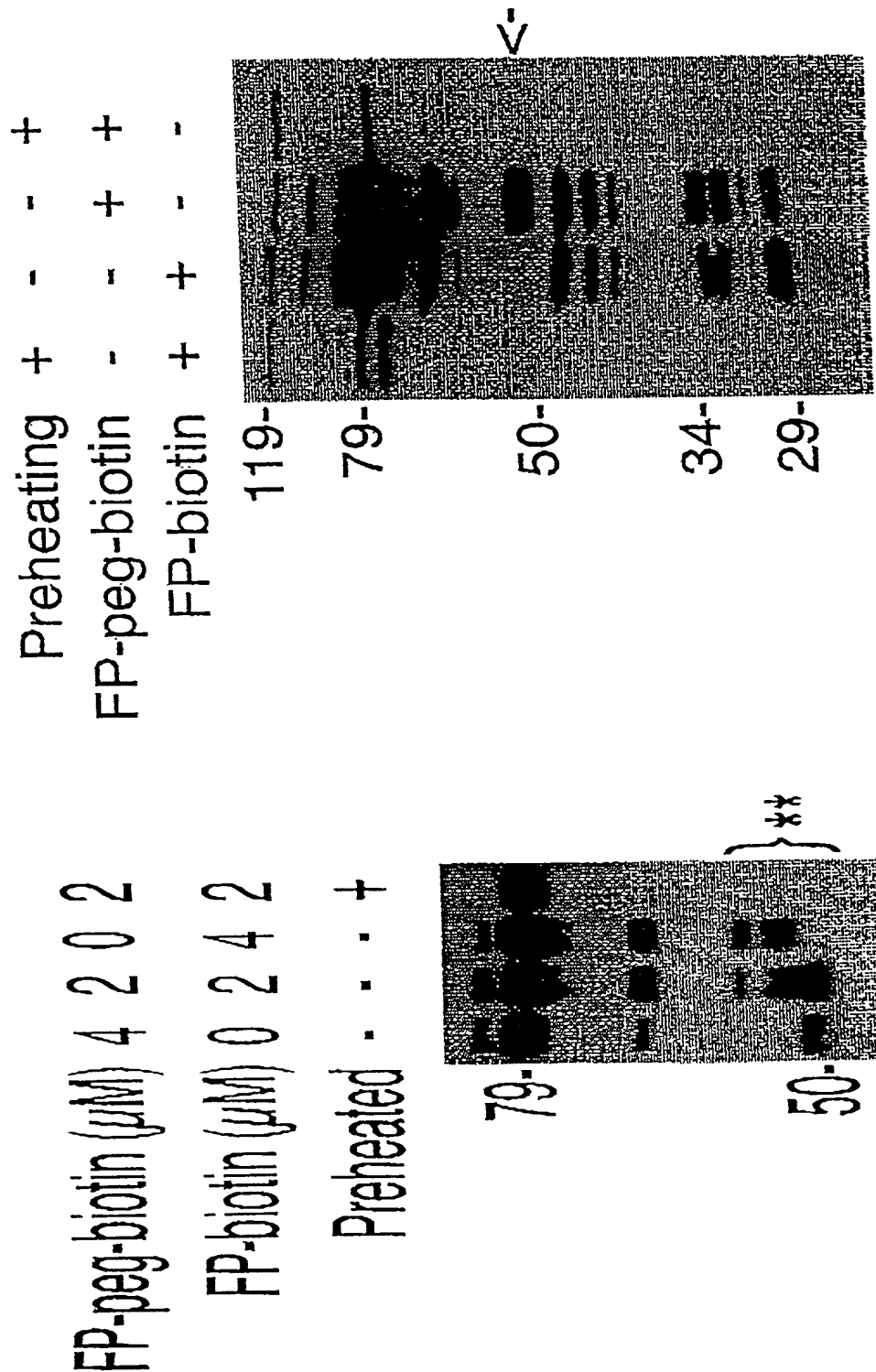


FIGURE 6

FIGURE 7

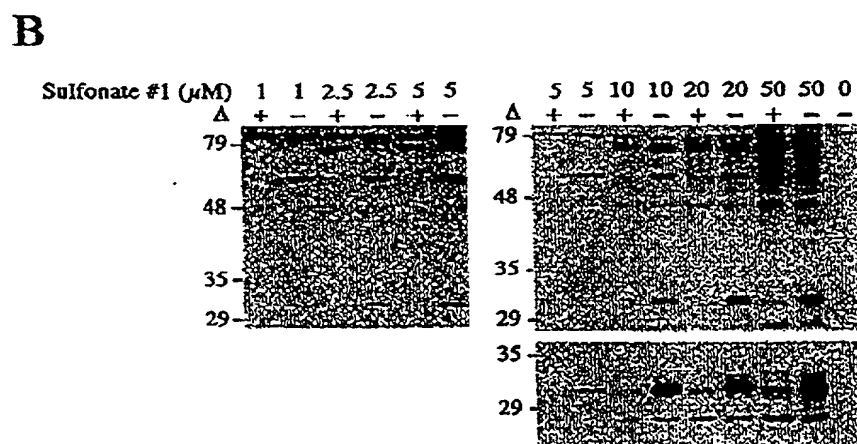
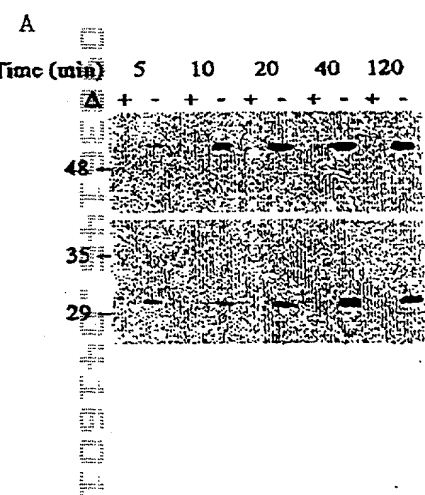
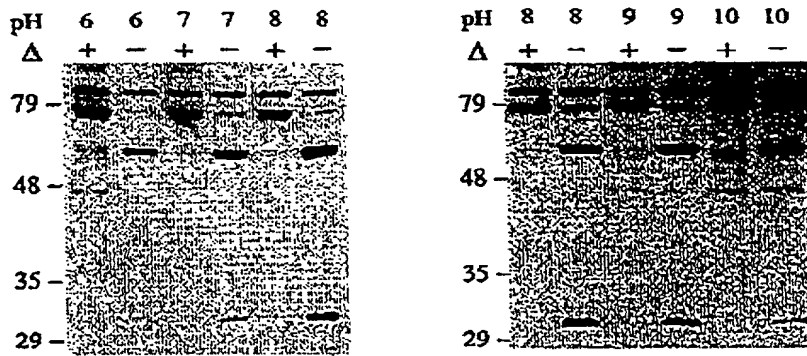


FIGURE 7

C



D

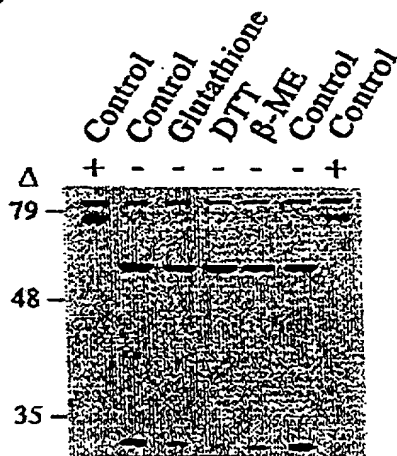


FIGURE 8

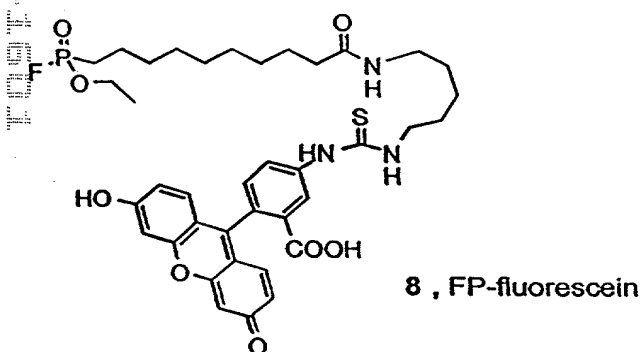
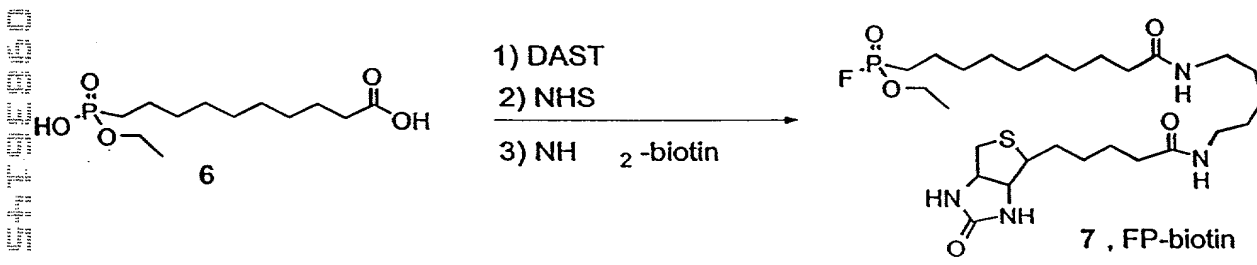
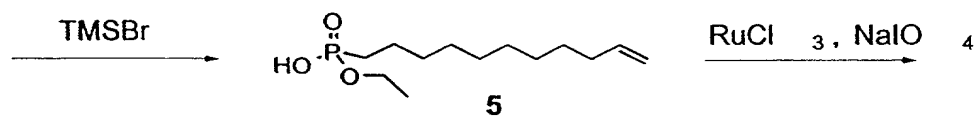
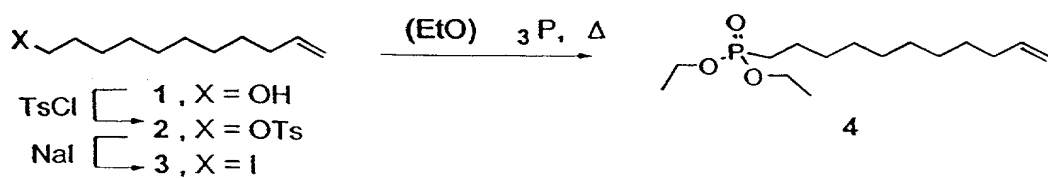


FIGURE 9

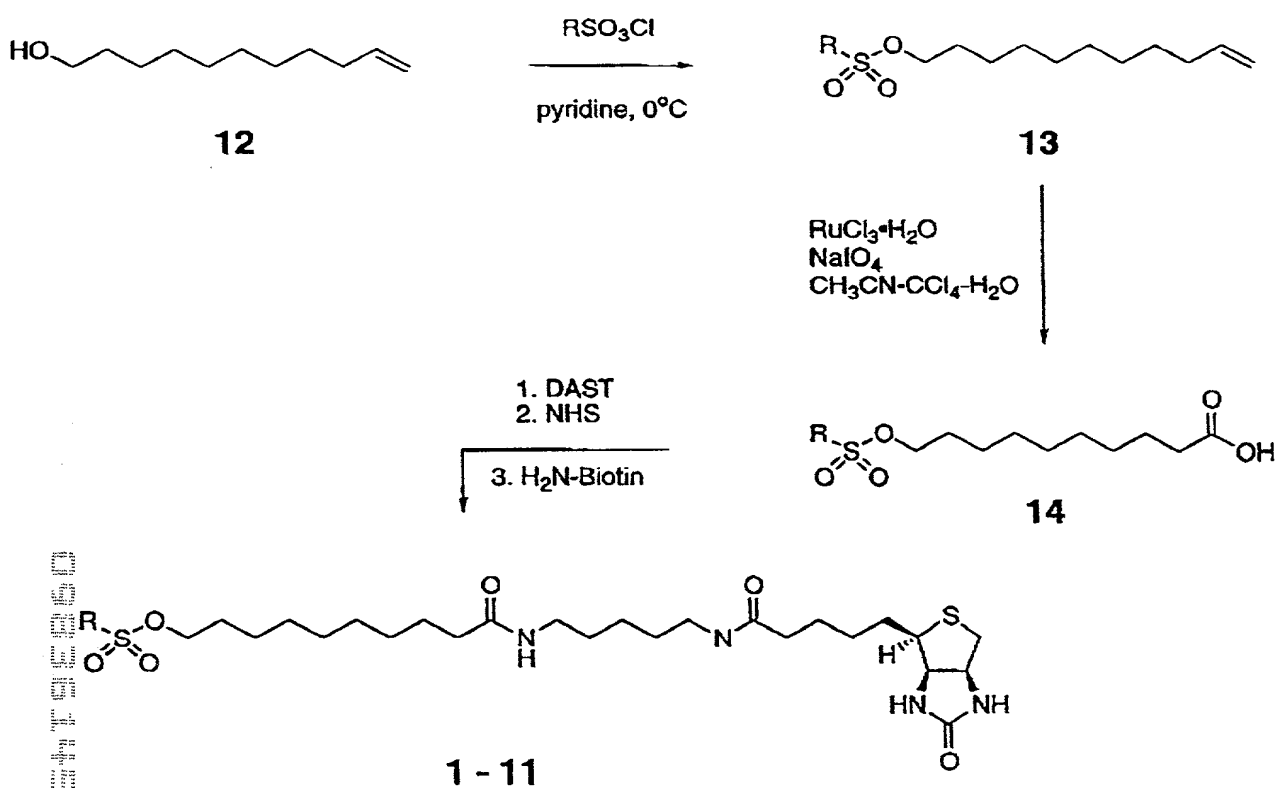
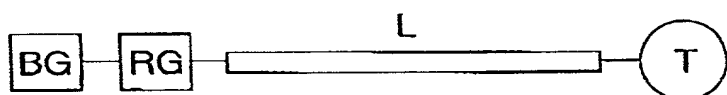


FIGURE 10

A.



B.

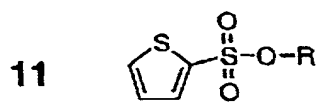
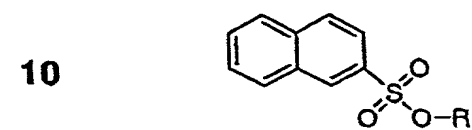
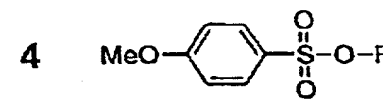
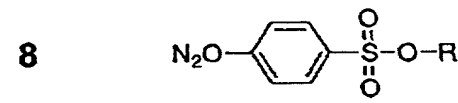
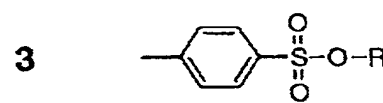
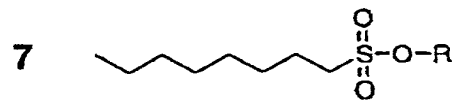
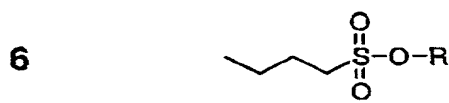
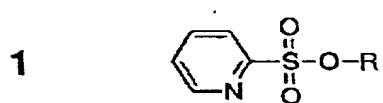
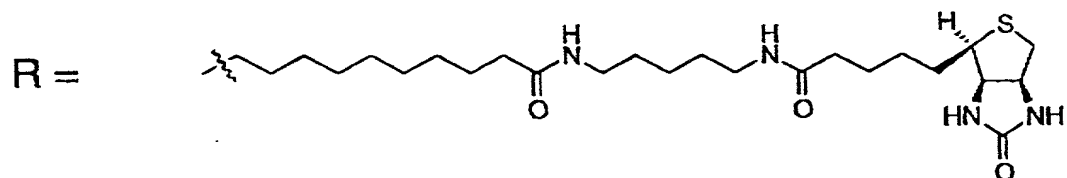
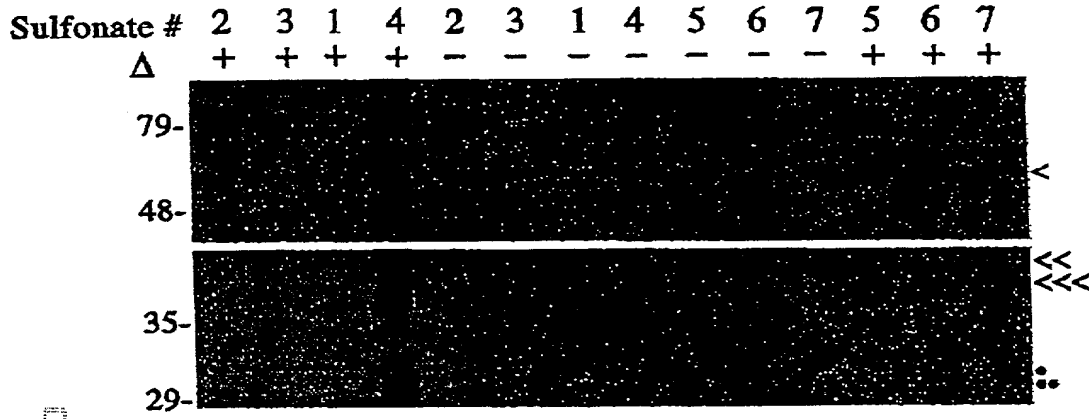
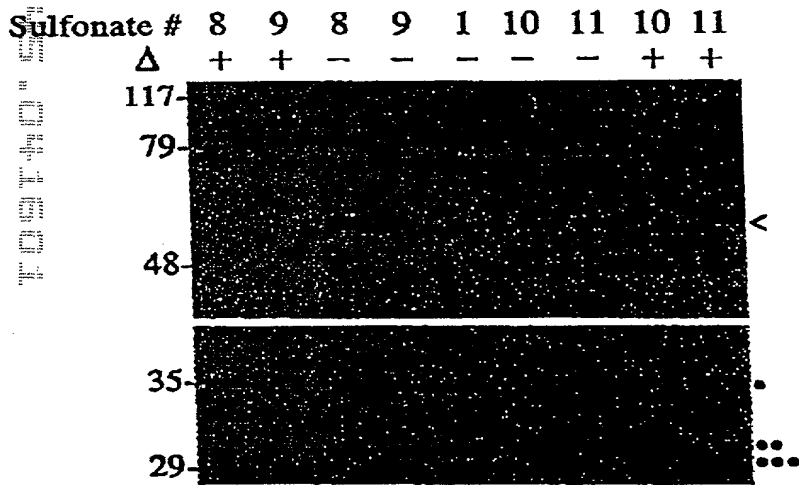


FIGURE 11

A

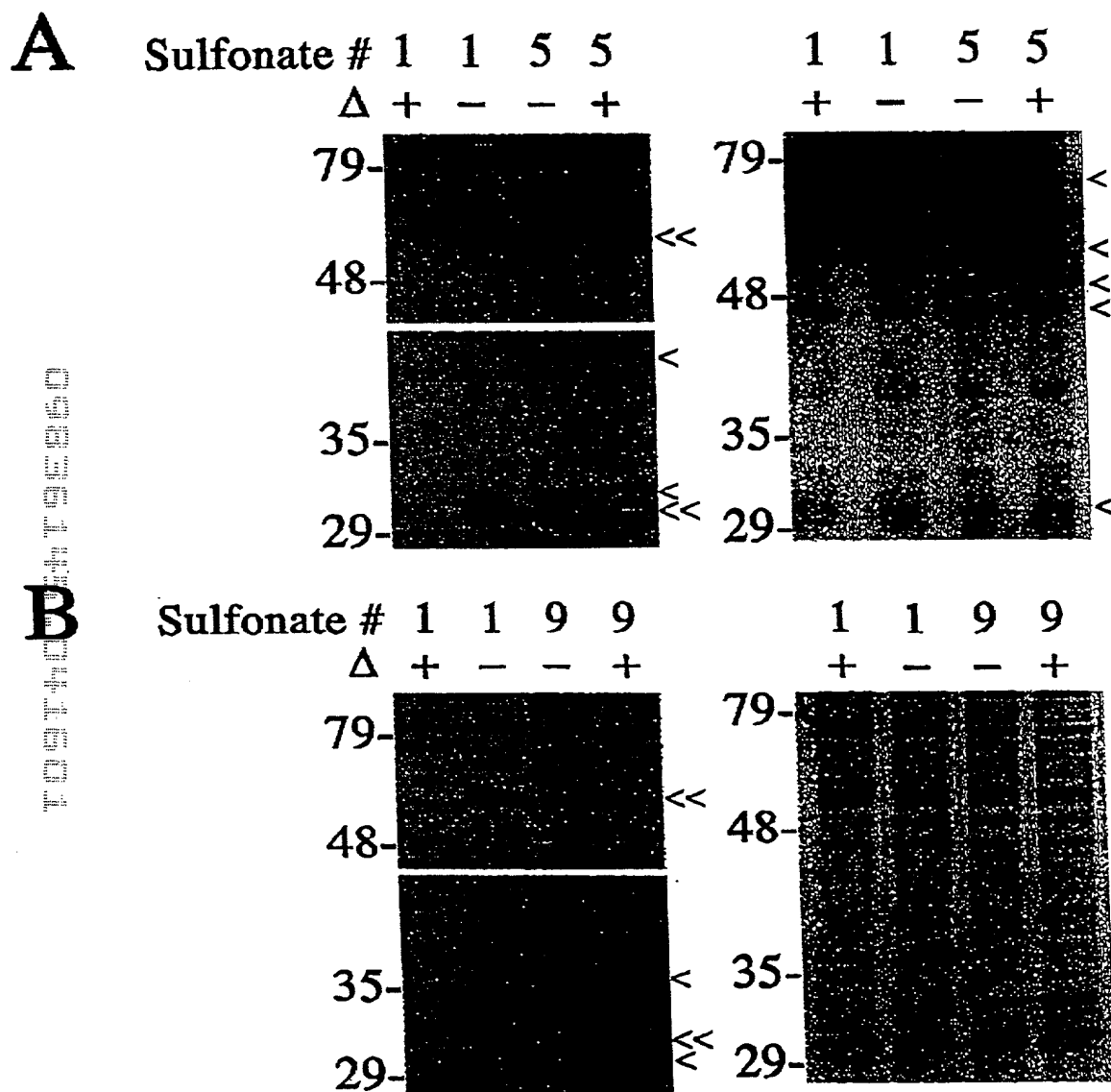


B



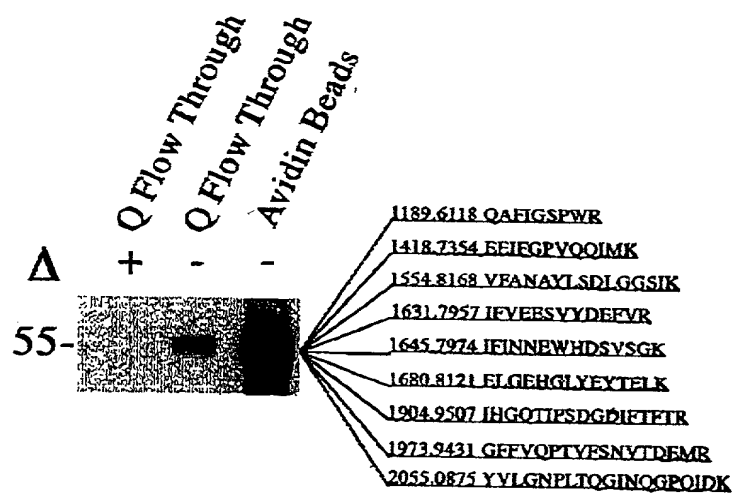
F05T40" 09E860

FIGURE 12

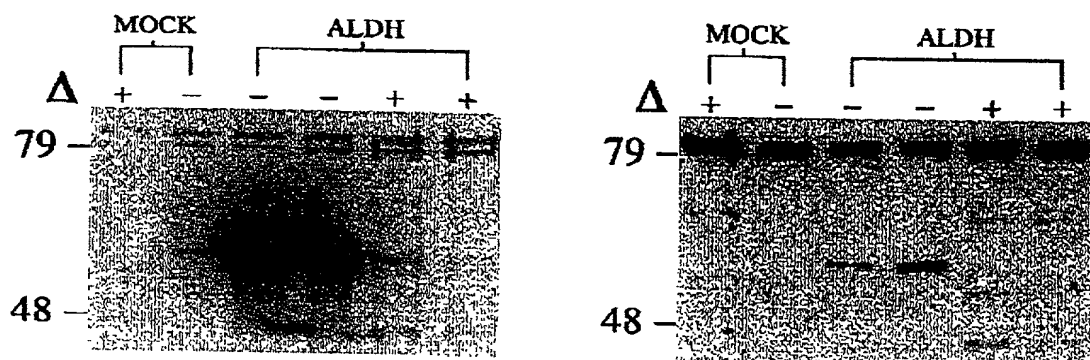


A

FIGURE 13



B



C

BL-21 Cells - - + +
Testis Proteome + + - -
 Δ + - + -

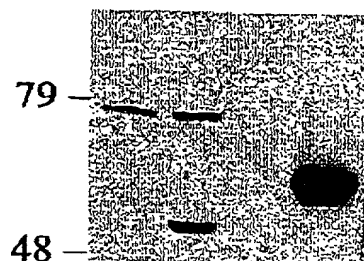
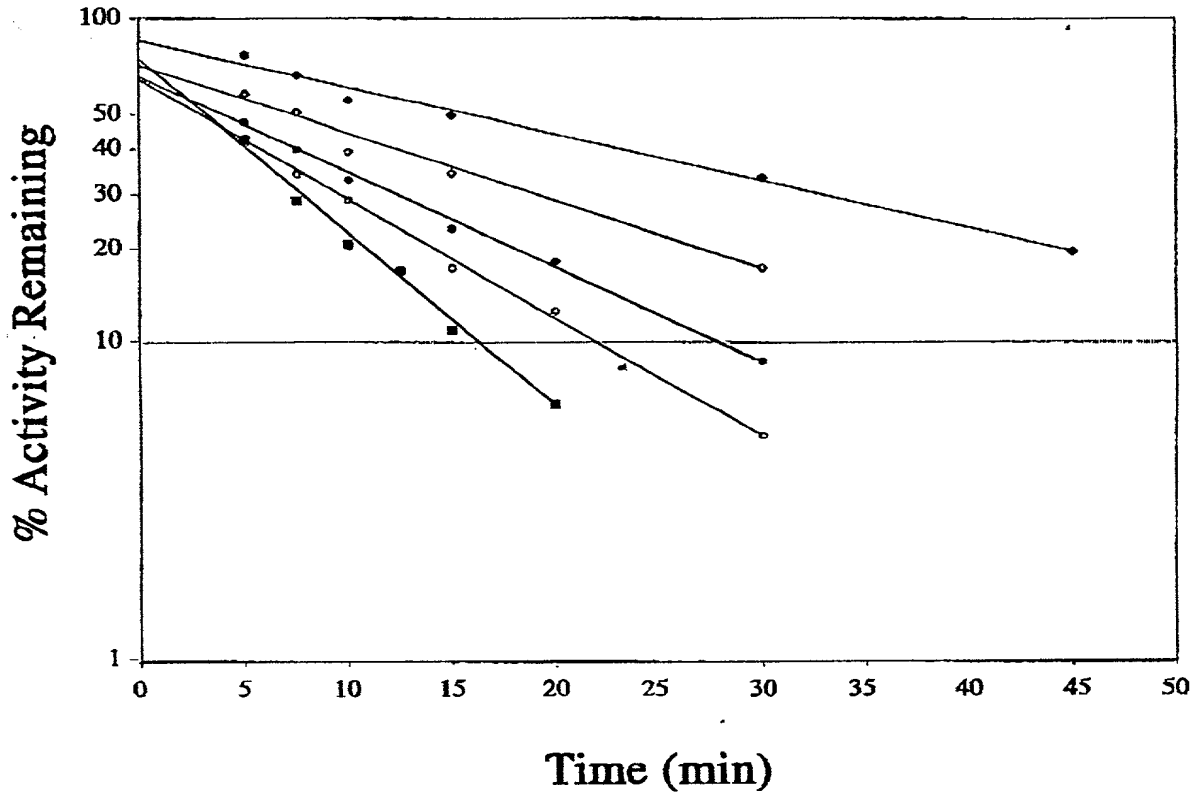


FIGURE 14

A



B

| | | | | | | | | |
|-------------------------|---|---|----|----|----|----|----|----|
| Competitor # | - | - | 15 | 17 | 16 | 15 | 17 | 16 |
| [Competitor (μ M)] | 0 | 0 | 5 | 5 | 5 | 50 | 50 | 50 |
| Δ | + | - | - | - | - | - | - | - |

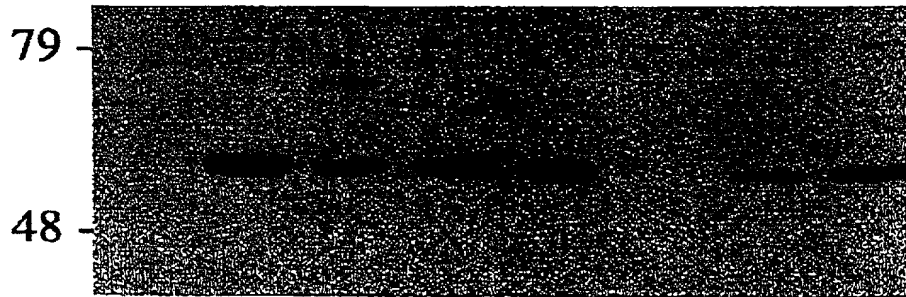
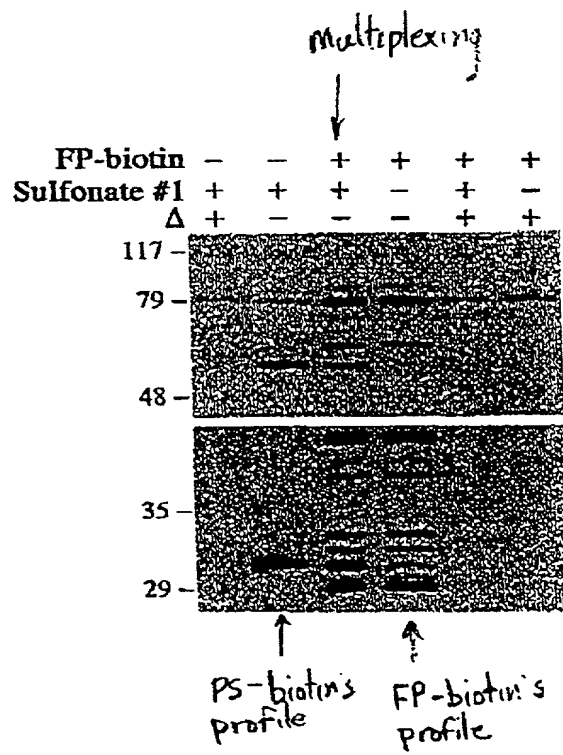
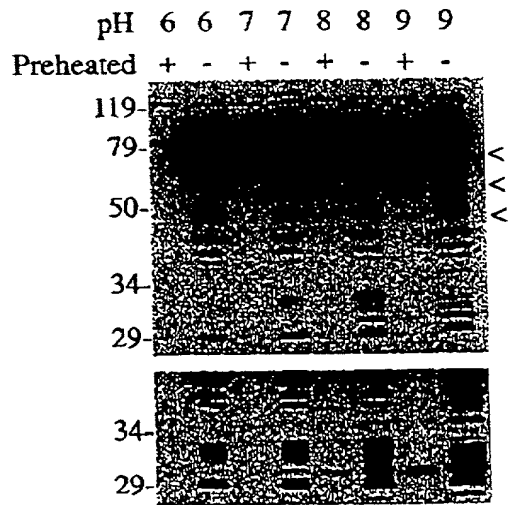


FIGURE 15

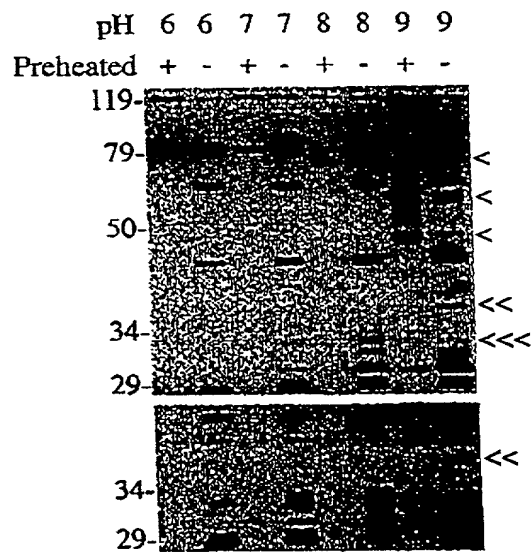


20240" 64T6E260

FIGURE 16



FP-peg-biotin



FP-biotin

FIGURE 17

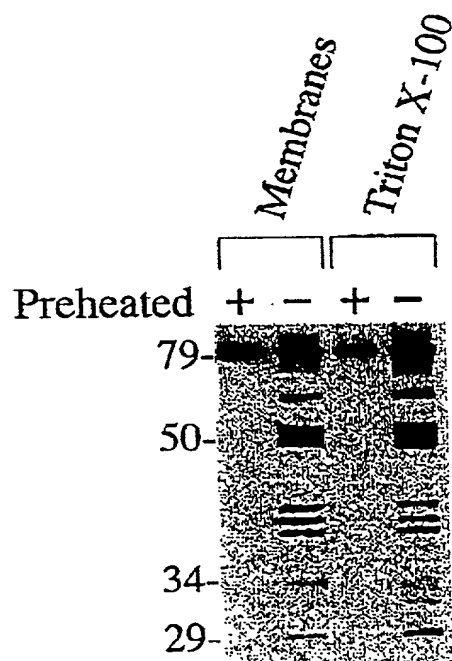
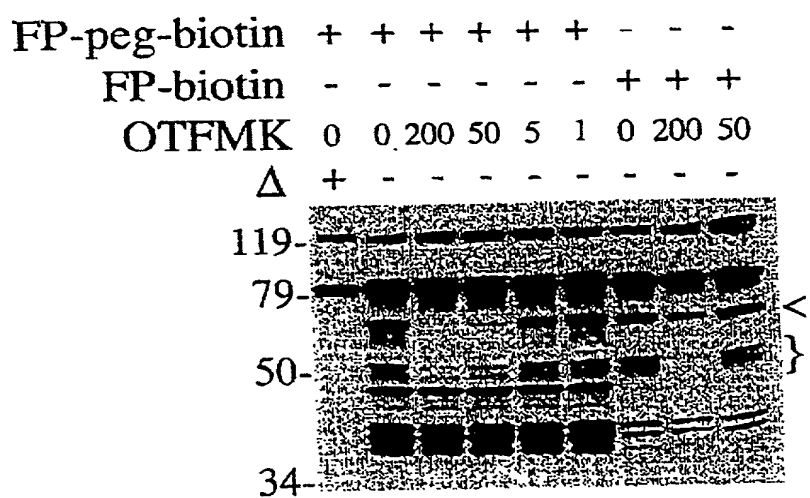


FIGURE 18



10310" 64198860

FIGURE 19

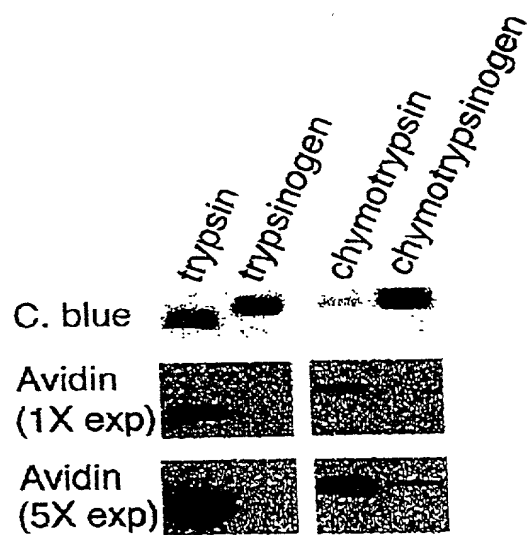


FIGURE 20

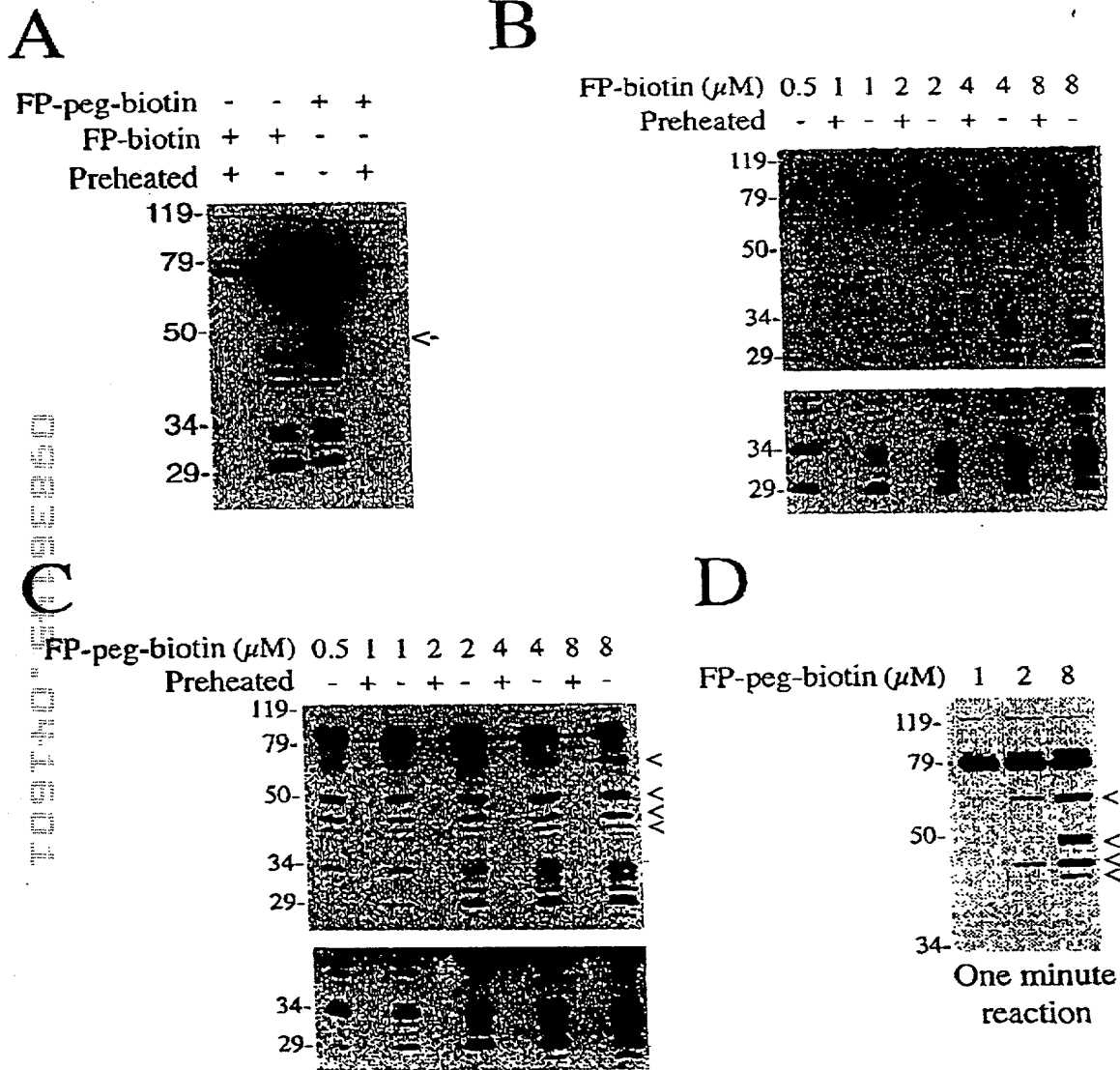
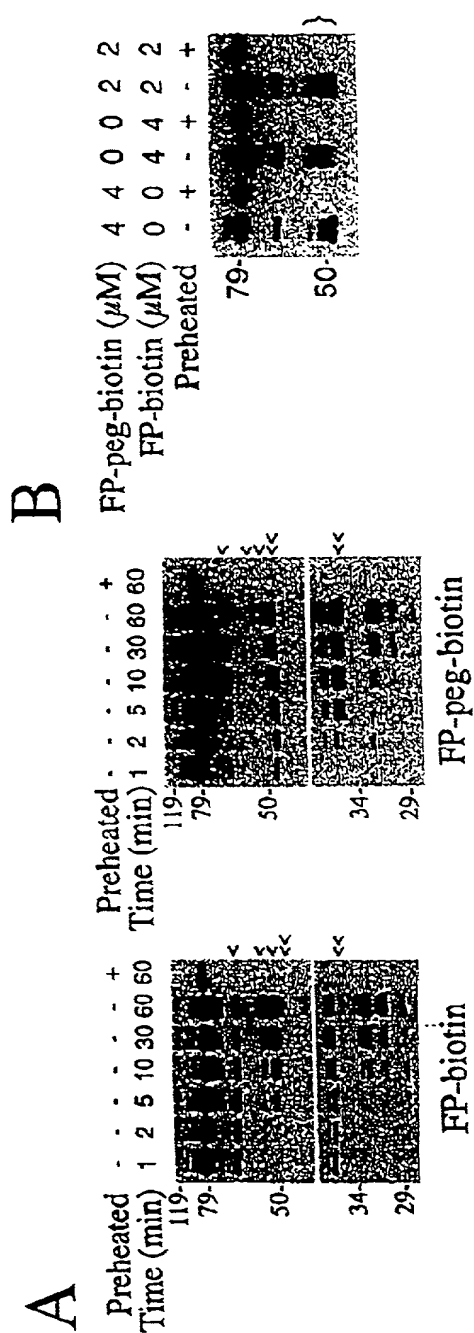


FIGURE 21



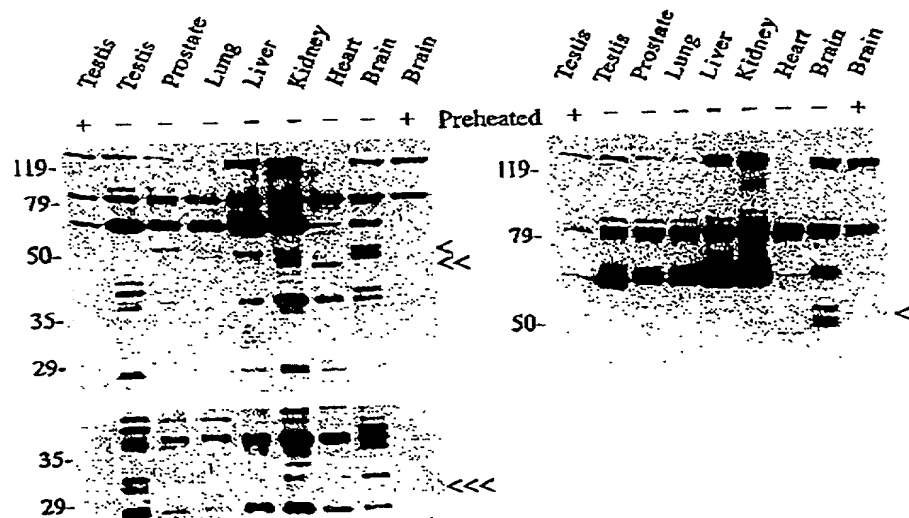
[illegible]

FIGURE 23

